

Results: Twenty patients were enrolled and treated with the Paradise System. The mean age at baseline was 54 ± 9 ; 81 % of the patients are male. The average number of anti-hypertensive medications at baseline was 5.4. The majority (72%) of patients were on spironolactone at baseline. 50% of patients had changes to their medications in response to BP changes during the 6 month follow-up period. Mean office SBP was 167 ± 18 mmHg and mean ambulatory SBP was 157 ± 14 mmHg at baseline. Of responders, the mean decrease in office SBP at 6 months was -41 ± 25 and the mean decrease in ambulatory SBP was -27 ± 22 at 6 months. At 1 month, MSNA decreased by 17%; the decrease in MSNA correlated with a decrease in BP ≥ 10 mmHg in 4 of 5 patients. The most commonly reported adverse event was procedural-related pain. There have been no reports of new onset renal artery stenosis.

Conclusions: The REALISE trial demonstrates that blood pressure can be safely reduced in patients with moderate resistant hypertension. Ultrasound renal denervation may provide benefit in a subset of patients despite active on-going medical management.

TCT-418

24h Ambulatory Blood Pressure (ABPM) Change After Using The New Symplicity Spyral Renal Sympathetic Denervation Device In Patients With Resistant Hypertension – First Results From The Halle-RDN-Registry

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Background: Despite the widely discussed unfavorable outcome of the SymplicityTM HTN 3 trial, several independent trials and registries have shown a blood pressure (BP) lowering effect in the majority of patients treated with a renal denervation (RDN) device. So far, current available data are almost entirely based on the SymplicityTM Flex System, a second-generation RDN device. Although well established and approved, it revealed several limitations like high time consumption, high rigidity and often a more or less random ablation pattern. The next generation SymplicityTM Spyral device has been designed to overcome many of these shortcomings by using multiple electrodes strung on a helical shaped catheter. However, the question about the effectiveness of the new system still remains.

Methods: Our study carefully investigated the ABPM response to RDN in a cohort of 29 consecutively treated patients with resistant hypertension using the Spyral device. Baseline values included a mean age of 67 ± 9.8 years, BMI of 31.3 ± 4.4 Kg/m², 48% women, 56% diabetic, 29% coronary artery disease and 5.4 ± 1.2 antihypertensive medications. A 24h BP monitoring was recorded in every patient 24h before as well as 24h and 3 months after RDN. BP readings were then averaged according to daytime (7:00am–22:00pm), nighttime (22:00pm–7:00am) and 24 hours intervals. All data were statistically analyzed using mixed models with repeated measurements.

Results: In treated patients mean averaged systolic 24h BP was reduced by 14.5 ± 4.6 mm Hg ($p < 0.005$; $n = 29$) during the first 24 hours. A similar effect on diastolic BP was observed: 4.9 ± 2.26 mmHg ($p < 0.05$). First analyses of 17 patients reaching the 3 months follow-up visit reveal a sustained systolic (7.3 ± 2.39 mm Hg, $p < 0.05$) as well as diastolic (4.8 ± 4.46 mm Hg, $p < 0.05$) ABPM reduction, without further decrease – on the contrary a slight relapse to higher BP was seen.

Conclusions: Using the multi-electrode SymplicityTM Spyral renal denervation device did not only improved steerability, ablation pattern and procedure time. It also seems to show a significant immediate as well as persisting reduction of systolic and diastolic ABPM.

TCT-419

Ethanol-Based Renal Sympathetic Denervation: Current Approaches

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Background: Ethanol (EtOH)-induced renal sympathetic denervation (RDN) has been described. We compare the results of percutaneous vs. endovascular infusion of EtOH.

Methods: MR-guided injection of 5 or 10 ml of EtOH per renal artery to the peria-arterial space was performed in pigs, with 4-week renal norepinephrine (NE) and histopathology data. In the same model, the Peregrine System™ was used to infuse 0.15, 0.30 or 0.60 ml of EtOH to the peri-vascular space of each renal artery. Histopathology, NE assay and immunostaining were performed at 2 weeks and 3 months. In a clinical setting, a CT-guided injection of EtOH (10 ml) was reported, and a safety and feasibility study (18 patients) is ongoing with the Peregrine System (0.30 ml EtOH).

Results: In pigs, 5 or 10 ml MR-guided EtOH injections yielded NE reductions of 0% and 53% vs. controls. The 5 ml EtOH produced no changes in renal nerve histology. The 10 ml injection resulted in neural degeneration, perineural fibrosis; hydro-nephrosis and kidney adhesions were observed. By comparison, pigs treated with micro-doses (endovascular) of EtOH, renal NE, neurofilament protein and tyrosine hydroxylase were all reduced in a dose-dependent manner, and circumferential sympathetic nerve injury (2–10 mm depth from intima) was observed at all doses. Renal NE dropped by 58%, 78% and 88%. No significant vascular wall changes or other systemic or anatomic pathologies were reported. The patient treated with CT-guided injection of EtOH (10 ml) office blood pressure (OBP) and ABPM were lowered by 29/14 of 15/8, respectively, at 4 weeks, with no adverse anatomical changes. No adverse events and either no pain or transient pain (< 2 min) were observed with the Peregrine System using 0.3 ml EtOH (18 patients). At 4 weeks, the

OBP dropped an average of 27/11, while antihypertensive medications were reduced from 3.2 to 2.1.

Conclusions: EtOH delivery into the peria-arterial space appears to be safe and feasible for RDN. In preclinical testing, micro-volumes delivered via a specialized endovascular catheter enabled a superior treatment than a percutaneous technique. The observations of minimal pain, safety and early efficacy with this approach in a clinical setting, are encouraging.

TCT-420

Safety and Performance of the Next Generation EnligHTN Renal Denervation System in Patients with Drug-resistant Hypertension: 12-Month Results From a First-in-Human Multicenter Study

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Background: Catheter-based renal artery denervation therapy has become established as a therapeutic option in patients with resistant hypertension. We further investigated the safety and performance of the next generation EnligHTN™ Renal Denervation System (St. Jude Medical) in patients with drug-resistant hypertension.

Methods: The EnligHTN Renal Artery Ablation Catheter has 4 electrodes attached on a basket mounted at the tip of the catheter. The next generation EnligHTN RF Ablation Generator utilizes a novel algorithm for the delivery of 1 minute of radio-frequency energy, optimized for simultaneous delivery of therapy through all 4 electrodes, with an interactive, intuitive user interface. Renal denervation was performed on 39 patients across 6 centers meeting the following inclusion criteria: 18–80 years of age, a systolic BP ≥ 160 mmHg, an average daytime systolic ambulatory BP ≥ 135 mmHg, on three or more antihypertensive agents (including a diuretic). Renal artery CT angiography was repeated at 6 months in all patients.

Results: To date 37/38 patients have completed 6-months of follow-up post procedure. No serious device or procedure related adverse events have been observed as adjudicated by an independent Clinical Events Committee. There were no clinically significant changes in renal function through 6-months as observed in eGFR, serum creatinine, cystatin C, or urine albumin-to-creatinine ratio. 6-month office (and 24 hour ambulatory) BP reductions from baseline were $-25.2/-7.3$ ($-8.2/-2.0$) mmHg, which were statistically significant except for the ambulatory diastolic reduction. Renal artery denervation procedures were performed successfully in all patients, with an average of 4.33 ablation sets and 15.85 ablations performed per patient. The mean total ablation catheter insertion-to-removal time was 22.38 min and mean ablation time was 4.33 min per patient.

Conclusions: Accumulated 12-month results from all sites will be presented. After 6-months follow-up in this first-in-human study, we conclude that data demonstrates the next generation EnligHTN Renal Denervation System continues to be safe, rapid, and effective in the treatment of patients with drug-resistant, uncontrolled hypertension.

TCT-421

Renal denervation in hypertensive patients: effects on neurohormonal activation and cardiac natriuretic peptides

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Background: Renal denervation is an emerging treatment in patients with resistant arterial hypertension. Neurohormonal activation (catecholaminergic and renin angiotensin aldosterone systems) play an important role in hypertensive patients; B-type cardiac natriuretic peptides have been demonstrated as useful biomarkers of both neurohormonal activation and cardiovascular overload.

Aim: To investigate effects of renal denervation on biomarkers of neurohormonal activation and NT-proBNP serum values.

Methods: 6 patients with resistant hypertension (mean value $> 140/90$ mmHg at 24 hours blood pressure monitoring despite use of three or more antihypertensive medications) underwent renal denervation. Norepinephrine (NE), plasma renin activity (PRA), aldosterone (A) and NT-proBNP were collected at baseline (B), 1 day (1D) and 1 month (1M) after the procedure. Patients underwent 24 hours blood pressure monitoring at B, 1D and 1M after the procedure. Any change in antihypertensive medications was made after the procedure.

Results: All procedures were performed without complications. Mean age 64 ± 12 years (range 43–75), 5 patients males. Diuretics were used in 6 out of 6 patients. Systolic (138 ± 6 at 1M vs. 150 ± 8 at 1D and 151 ± 6 mmHg at B, $p < 0.01$), diastolic (73 ± 10 at 1M vs. 79 ± 12 at 1D and 81 ± 12 mmHg at B, $p < 0.01$) and mean (94 ± 6 at 1M vs. 102 ± 7 at 1D and 105 ± 6 mmHg at B, $p < 0.01$) arterial pressure values, all

decreased at 1M after renal denervation procedure. NT-proBNP (126; 87-178 at 1M vs. 353; 178-490 at B, $p < 0.01$), NE (441; 198-598 at 1M vs. 752; 629-850 at B, $p < 0.01$) and A (98; 75-128 at 1M vs. 165; 114-269 at B, $p < 0.01$) all decreased at 1M after renal denervation procedure, while PRA did not change. Percentual decrease of mean arterial pressure was strictly correlated with both percentual decrease in NT-proBNP ($r = 0.742$, $p < 0.05$) and NE ($r = 0.924$, $p < 0.01$).

Conclusions: Biomarkers of neurohormonal activation and cardiovascular overload such as norepinephrine, aldosterone and B-type natriuretic peptides appear positively affected by renal denervation procedure in resistant hypertensive patients. Interestingly, decrease of such neurohormones strictly reflect decrease in arterial pressure values.

TCT-422

Transluminal Imaging of Renal Nerves using Optical Coherence Tomography

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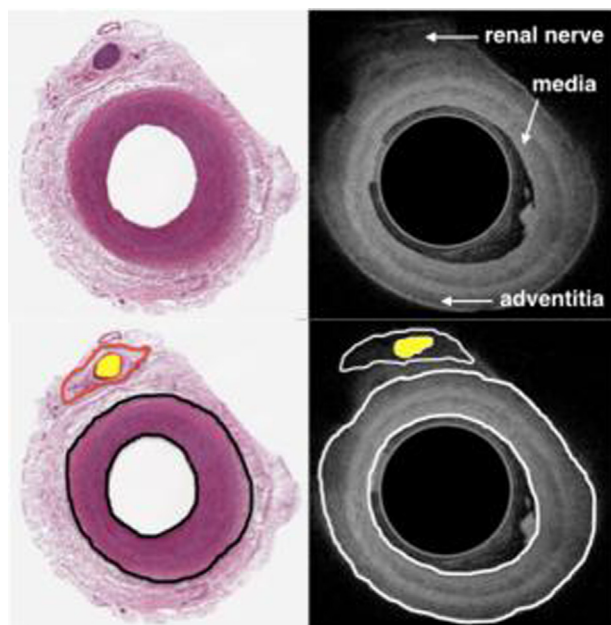
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Background: Renal denervation for refractory hypertension has received considerable interest in recent years. Initial clinical data demonstrated a significant reduction in blood pressure following radiofrequency ablation of the renal nerves. However, the recent clinical trial SYMPPLICITY HTN-3 failed to meet efficacy endpoints. One theory for insufficient efficacy is incomplete ablation of the renal nerve. In this study we test if the renal nerves, in particular the main renal nerve bundle, could be visualized through the renal arterial wall using optical coherence tomography (OCT) to guide more precise ablative energy.

Methods: Specimens included fresh porcine abdominal aortas with kidneys attached. The Ocelot catheter (Avinger Inc, Redwood City, CA) using a 1300 nm OCT swept source laser was inserted through the aorta and advanced to the renal artery. Following OCT imaging, the tissue was fixed, sectioned (5 μ m thick), and stained with hematoxylin and eosin.

Results: Figure 1 displays an OCT image from within the renal artery juxtaposed with the identical histologic arterial section. OCT accurately identifies the location of the renal nerve bundle via the optical properties of the surrounding myelin, which creates delineated borders when compared with neighboring adventitia.

Conclusions: OCT is gaining increased use within cardiovascular imaging and therapy. The clear identification and localization of the renal nerve bundle via OCT may prove useful for targeted ablative therapies, including renal denervation.



TCT-423

The Paradise Renal Denervation System: Initial Clinical Results from the ACHIEVE Study

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Background: While the efficacy of a first generation radio frequency renal denervation device has recently been challenged, new technologies are available designed to optimize procedural success. The Paradise® Renal Denervation System (ReCor Medical, Palo Alto, CA) delivers ultrasound energy to perform targeted circumferential denervation of the renal sympathetic nerves in order to reduce blood pressure (BP) and secondary end-organ damage.

Methods: The ACHIEVE study is a prospective, multi-center, non-randomized, post-market study to evaluate the clinical outcome of renal denervation with the Paradise System in patients with resistant hypertension. Major exclusions include renal artery stenosis and moderate to severe renal insufficiency. Patients were treated with the Paradise system and followed for 12 months. Non-invasive imaging using CR or MRI was performed at 12-months to assess renal artery patency. Safety and efficacy endpoints were evaluated including renal complications, changes in office and ambulatory BP, changes in medication and Quality of Life measures.

Results: Eight sites in Europe are actively recruiting in the ACHIEVE study. Mean age at treatment is 63 ± 11 years (range 38-86 years) and 56% of patients are male. At baseline, mean office systolic BP is 177 ± 20 mmHg ($n=67$) and mean ambulatory systolic BP is 156 ± 13 mmHg ($n=62$). Early data demonstrate a significant decrease in systolic office BP at 30 days post treatment (average BP change of -16 mmHg, $n=47$, $p < 0.005$), sustained at both 3 and 6 months. Patients with baseline office BP ≥ 160 mmHg had larger overall drops in systolic BP versus those whose baseline BP was < 160 mmHg (-19 ± 29 mmHg; $n=29$; $p < 0.005$ versus 2.1 ± 20 mmHg, $n=8$). Average 24-hour ambulatory blood pressure changes are also sustained over follow-up with an average decrease of -7 mmHg recorded at both 3 and 6 months post treatment. No procedure related serious adverse events occurred in the initial follow-up. Updated results will be presented at the meeting.

Conclusions: Initial ACHIEVE study results demonstrate that the Paradise System is safe and effective in patients with resistant hypertension. Early data suggests that a reduction in BP occurs within 30 days and is sustained.

TCT-424

Unfavourable Anatomy Of Renal Arteries Should Not Be An Exclusion Criteria For Renal Sympathetic Denervation

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Background: Catheter-based renal sympathetic denervation (RDN) is indicated for treatment-resistant arterial hypertension (systolic pressure ≥ 160 mmHg on ≥ 3 anti-hypertensive drugs). A radiofrequency catheter induces controlled thermal sympathetic nerve destruction in the renal arteries resulting in lowered sympathetic tone and blood pressure (BP). According to the Symplicity trials, patients with anatomical abnormalities of the renal arteries like additional arteries or early bifurcations have not been eligible for this treatment.

Methods: Our study carefully investigated the ambulatory 24 hour blood pressure (ABPM) response to RDN in a cohort of 181 consecutively treated patients with resistant hypertension. A 24h BP monitoring was recorded in every patient 24h before as well as 24h, 3 and 6 months after RDN. According to the renal artery anatomical findings, the following 5 groups have been identified: normal anatomy, additional arteries, early bifurcation (segmental bifurcation < 15 mm from the ostium), tortuosity and atherosclerotic plaque. All data were statistically analysed with repeated measures ANOVA and Greenhouse-Geisser correction if indicated.

Results: In treated patients (age 63 ± 9.6 years, BMI 31.9 ± 5.8 Kg/m², 48% women, 48% diabetic, 19% coronary artery disease and 5.7 ± 1.8 antihypertensive medications) mean averaged systolic 24h BP was significantly reduced in every anatomical group during the first 24 hours. Patients with additional renal arteries or early bifurcations seem to have a more sustained systolic BP reduction at 3 and 6 months compared to tortuous renal arteries, evidence of plaque or normal anatomies. Here a relapse to baseline BP was seen.

Conclusions: Patients with resistant hypertension and unfavourable renal vascular anatomy seem to benefit at least to an equal extent from RDN as patients with normal renal arteries. However, our data suggest, that tortuosity and atherosclerotic plaque may be a negative predictor of BP response, whereas early bifurcations and additional renal arteries appear to be positive predictors.